Advanced Research + Invention Agency ARIA

Precision Neurotechnologies for Human Therapeutics

Call for proposals

Date: 10 July 2024

V3.0 (updated 30th July 2024)

Advanced Research + Invention Agency ARIA

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SECTION 1: Programme Thesis and Overview

This solicitation is derived from the programme thesis Precision neurotechnologies for human therapeutics, in turn derived from the ARIA Opportunity Space: Precisely interfacing with the human brain at scale.

Introduction

Brain disorders are the cause of an overwhelming social and economic impact: in 2019 they accounted for 21% of the global disease burden (compared with 7% for coronary heart disease), costing an estimated 530m disability adjusted life-years (DALYs) [1, 2]. Many of these conditions are **disorders of neural circuits**, involving a diversity of cell type, distributed across different brain regions, and with complex temporal dynamics. This programme aims to develop breakthrough technologies to interact with the central nervous system at the circuit-level and then apply these tools to demonstrate therapeutically relevant capabilities that are fundamentally not possible with existing approaches.

Background

It is becoming increasingly evident that targeted interaction with the human nervous system can improve the human condition across an incredibly wide range of disease states and cognitive domains. An existence proof is deep brain stimulation (DBS), which has been approved by the U.S. Food and Drug Administration to treat movement disorders such as Parkinson's disease and essential tremor [3], and neurological disorders such as epilepsy [4]. Emerging work suggests DBS can be effective for a much wider range of treatments than previously envisioned, including treatment-resistant depression [5], mood and anxiety disorders [6], post-traumatic stress disorder [7], substance addiction [8] and potentially even Alzheimer's disease [9], pointing towards a vast pool of the population that can potentially benefit from neurotechnologies.

Despite these promises — and despite significant momentum in areas such as brain-computer interfaces (BCIs) for people with severe motor impairments [10] — neurotechnologies have yet to see wide adoption and the space is vastly underserved relative to its potential impact. In the UK alone, fewer than 400 DBS surgeries are performed annually [11], and likely only a few dozen people worldwide have been implanted with high-bandwidth BCIs [12]. The core thesis of this programme is that to successfully treat the most common and complex neurological and neuropsychiatric

conditions at scale, we need platform neurotechnologies that interface with the human brain at the same level as the disorders themselves – the circuit level.

Many neurological and neuropsychiatric disorders are now thought to be disorders of *neural circuits* [13,14]. We define a circuit-level disorder as one where there is dysfunction between interconnected brain regions (macro-circuits) or within a brain region (micro-circuits). Another key circuit element is *cell type*: the human brain consists of billions of neurons that are organised into thousands of different cell types, each with distinct morphological, transcriptomic and functional properties. Neurons of different cell types within close proximity can drive radically different downstream functions and behaviours [15], and distinct cell types can often be involved in disorders [16].

Our current paradigm of electrical-based neuromodulation and readout struggles to interface at the circuit level: it is coarse-grained, has no controllable cell type specificity, and is challenging to scale across multiple brain regions and distinct circuit elements.

By uniting the frontiers of engineered biology with engineered hardware, this programme aims to develop breakthrough technologies capable of interfacing with the human brain at the circuit level, across distributed brain regions and with cell type specificity — a paradigm we term 'precision neurotechnologies'. We believe such *platform* precision neurotechnologies can alleviate the bottlenecks with existing therapies: accounting for disease heterogeneity, minimising side effects and ultimately unlocking significantly more effective treatments for a wider array of brain disorders and a much broader patient population. If this programme is successful, we envision a world in which personalised brain health care is available to everyone.

SECTION 2: Programme objectives

This programme seeks teams from across the R&D ecosystem that will be funded by ARIA across three Technical Areas:

+ **TA1:** Focused on the *development* of next-generation precision neurotechnologies to interface with the mammalian brain at the circuit level.
+ **TA2:** Focused on *applying* precision neurotechnologies to demonstrate therapeutically relevant capabilities that are not possible with existing approaches.
+ **TA3:** Focused on *understanding* the factors that will be critical for the adoption of future neurotechnologies, including:
    - Patient and broader stakeholder engagement and preferences.
    - Healthcare economics analyses.
    - Ethical issues related to neurotechnologies.

TA1 — Development of next-generation precision neurotechnologies

The primary goal of this Technical Area is to develop a suite of next-generation precision neurotechnologies to enable circuit-level access to the central nervous system, with cell type specificity and across distributed macro- and micro-brain circuits. A key guiding principle of this Technical Area is to fund a broad portfolio of early-stage technologies, including approaches that may not traditionally be considered 'neurotechnologies'. We particularly encourage approaches that leverage insights from biology, apply methods in biological engineering, or unite engineered biology with engineered hardware.

Advancing precision.
In Section 3, we define a 'precision' metric *P* to quantify how well a particular technology interfaces with neural circuits, which comprises two components: 'localisation' and 'scale'. We are seeking technologies that significantly advance *P* over the state-of-the-art. At the submission stage, applicants will be required to estimate *P* for their proposed technology and compare it to a relevant existing technology (see Section 3 for an example calculation). If successful, teams will be tasked with measuring *P* via ground truth methods. Note that *P* is intended to capture order-of-magnitude advances, and applications will not be assessed purely on this metric. Indeed, we anticipate and encourage proposed technologies to advance certain axes of the precision phase space, e.g. a technology X that significantly increases cell type specificity, or a technology Y that

significantly increases volumetric coverage of the brain. Above all, we will prioritise novel ideas and are looking to fund a portfolio of early stage technologies.

Readout & modulation.
TA1 is designed to develop high-performance *technology options*, so we anticipate teams focusing on novel one-way (readout *or* modulation) approaches. However, we will also consider technologies that can be used bidirectionally (readout *and* modulation), provided the combination doesn't sacrifice performance. If teams propose a neuromodulatory technology, it must be able to be controlled by an exogenous signal (e.g., to dose the treatment) or an endogenous signal (e.g., closed-loop operation based on neural signals or behaviour), and dose-response curves and readout-modulation latencies should be carefully characterised.

End deliverables:

+ Demonstrate the fundamental principle of operation.
+ Ground truth measurement of precision.
+ If the technology is device based, design and development of a miniaturised, portable, prototype.
+ Demonstrate successful operation of the system *in vivo*.
+ Full safety and efficacy characterisation.

We intend to fund 10–12 awards within this Technical Area with a budget of £2–4m for each project for a duration of up to four years. We have also budgeted to enable exceptionally promising TA1 technologies to transition to the TA2 track. Teams applying to this Technical Area must also consider the 'clinical translatability' requirements outlined below.

TA2 – Applying precision neurotechnologies

We strongly believe that to yield the greatest impact, precision neurotechnologies should be integrated into a measure-model-perturb cycle (see Figure 1) to: (1) record neural signals across relevant cortical and subcortical micro- and macro-circuits during both health and disease states; (2) build data-driven simulations of the brain to identify biomarkers of disease states and predict novel modulation targets that can (3) regulate the brain towards target healthy states.

The goal of this Technical Area is therefore to demonstrate that precision neurotechnologies, when combined with advances in computational simulations, will

unlock entirely new therapeutic capabilities. We plan to support up to three interdisciplinary teams to develop and leverage precision neurotechnologies to demonstrate the controllable, predictable, and reversible transition between novel brain states *in vivo*.

Computational simulations.
Recent work has shown it is possible to simulate the dynamics of brain networks and predict the effects of targeted electrical modulation [17]. Here, the goal is to go beyond prediction by using data-driven simulations to *generate new modulation patterns that can transition the brain to a desired target state* (see, e.g., [18] for a working description of 'brain state'). We expect this Technical Area to yield breakthroughs in new computational methods, for example in network theory [19], optimal control theory [20], linear dynamical systems [18], or nonlinear dynamical systems [21]. We conjecture that cell type-specific signals [22] distributed across distinct brain regions [21] will enable more accurate and practical simulations of brain activity.

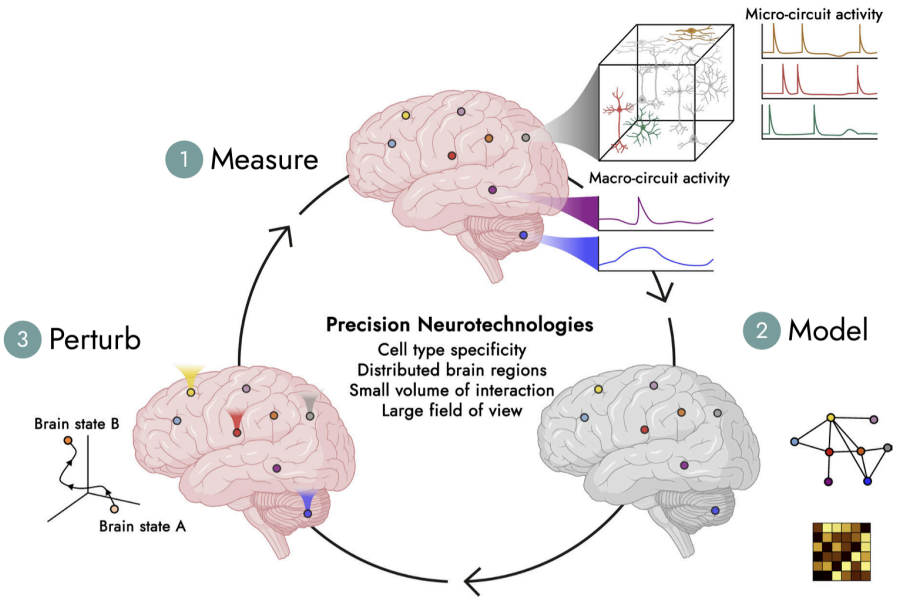

Figure 1. *Precision neurotechnologies can enable (1) a new lens into the functioning of the human brain, across brain regions (macro-circuits) and within brain regions (micro-circuits). This data will form the basis for (2) new models of the brain during disease states and in health which will enable the identification of (3) novel therapeutic targets to transition from brain state A to brain state B.*

Brain states.
Applicants should describe the particular set of brain states they wish to focus on, provided the states can be well-defined, the transitions between states verified via ground truth methods, and that the transitions are predictable and reversible. We particularly encourage brain states relevant to neurological and neuropsychiatric conditions, although we acknowledge the limitation of suitable animal models for many of these disorders.

New therapeutic capabilities.
In the application, teams should describe how their technology advances 'precision' and the new therapeutic capabilities their technology will unlock. This may include, but is not limited to:

+ More efficient brain state transitions (e.g., in time or applied energy).
+ The minimisation of unwanted side effects.
+ Transitioning to out-of-manifold states.
+ Longer-lasting therapeutic benefits.
+ Less invasive (i.e., more superficial) modulation targets.
+ Device-mediated plasticity.

Teams should also describe how they intend to assess these new capabilities and how they will benchmark their system against the relevant state-of-the-art technology.

Team composition.
We expect teams applying to this Technical Area to incorporate the necessary interdisciplinary expertise such as engineers (e.g., neuroengineers, bioengineers, electrical engineers), simulation experts (e.g., computational neuroscientists, computer scientists), experimental neuroscientists, veterinary expertise, and potentially even a clinical partner.

We anticipate proposed technologies to be either entirely new systems, whose fundamental principles of operation have not yet been demonstrated, or, due to the more demanding *in vivo* requirements, approaches that include refinements, augmentation, miniaturisation, and surgical adaptation of technologies whose fundamental principles of operation may have already been demonstrated. In the latter case, we note that we are looking for fundamentally new systems and not the direct application of existing technologies. For example, applicants may have already demonstrated the fundamental principle of operation of device X and then re-engineered the device in a novel and inventive way to significantly advance precision.

End deliverables:

+ Demonstrate the fundamental principle of operation (if not already demonstrated).
+ Ground truth measurement of precision.
+ If the technology is device based, design and development of a miniaturised, portable, prototype.
+ Demonstrated controllable and reversible transition between a set of brain states *in vivo* with correlation ρ between expected and measured states ρ>0.6 (see Section 3).
+ Full safety and efficacy testing in the most relevant near-human model (e.g. cadaver, large animal, etc).

We intend to fund up to three awards within this Technical Area with a budget of £8–10m for each project, for a duration of up to four years.

Animal models in TA1 and TA2

While the overall goal of the programme is to develop human-compatible neurotechnologies, the target endpoint of TA1 and TA2 is demonstration in a suitable preclinical animal model. We are interested in technologies that can be demonstrated in non-mouse animal models to help support clinical translation. Specifically:

- For Technical Area 1, proposals demonstrating feasibility in mouse models are acceptable, with the demonstration of technologies in non-mouse models advantageous but not essential.
- For Technical Area 2, proposals relying solely on mouse models are welcome but preference is given to those demonstrating technologies in non-mouse models.

Under exceptional circumstances, we will consider technologies whose endpoint is first-in-human, provided this doesn't sacrifice technology performance.

Animal testing and clinical trials

You can find more information on ARIA's policy on animal testing here, and clinical trials here.

If you intend to carry out animal testing or clinical trials as part of the proposed project you will be required to answer some additional questions in your proposal submission.

These questions can be found in the concept paper guidance here and full proposal guidance here.

Clinical translatability in TA1 and TA2

Even though this programme is developing early-stage technologies, we believe there are several steps that can be taken at this early stage to support the ultimate goal of clinical translation. We therefore require TA1 and TA2 applicants to:

+ Consider and describe how their technologies will be used with humans. We are particularly interested in approaches that leverage novel surgical or delivery methods, including (but not limited to) injectables [23], skull implants (compatible with standard burr hole geometries) [24], and endovascular stents [25]. Also, consider potential explantability.
+ Specify the particular condition they anticipate applying their technology to and outline the performance metrics that need to be met. This is not meant to be binding, and if new opportunities emerge during the course of the programme, ARIA will work with teams and a clinical advisory council to refine their technology for different applications.
+ Assess and report the safety of their technology via the most relevant tests (e.g., histology and toxicology [26, 27]), as well as the longevity of their technology. Midway through the programme, ARIA intends to select contract research organisations to standardise and perform these tests for the most promising technologies.

Clinical advisory council

ARIA will assemble a 'clinical advisory council' comprised of clinicians, healthcare professionals and other experts with relevant expertise across various neurological and neuropsychiatric conditions. The clinical advisory council will meet with funded teams multiple times a year to provide guidance on the translation of ARIA funded technologies. The council will provide guidance and cannot make funding decisions.

TA3 — Understanding future adoption of precision neurotechnologies

Alongside supporting research into technology development, ARIA recognises that there are many other factors critical to the future adoption of precision neurotechnologies within the UK and beyond. We are therefore soliciting research into these factors, with the goal of developing concrete and actionable recommendations to be shared with the wider neurotechnology community. Such topics may include, but are not limited to:

+ Working with people with lived experience of neurological and neuropsychiatric disorders to better understand preferences related to advanced neurotechnologies.
+ Engaging with stakeholders more broadly across the ecosystem, e.g., family members, other long-term caregivers, clinicians (including those on the referral path), surgeons, and regulators.
+ Research into healthcare economics aspects of developing, implementing, and sustaining advanced neurotechnologies in a healthcare system.
+ Research into ethical issues related to neurotechnologies, exploring the moral, legal, and social implications, and providing concrete guidelines, frameworks, and policies to ensure responsible development and use of neurotechnologies.

We intend to fund multiple projects within this Technical Area, up to a maximum of £400k each, and for a maximum of four years (although we anticipate multiple smaller awards for shorter lengths of time). ARIA may also open a second TA3 call at a later stage to focus on specific challenges identified within the programme.

SECTION 3: Technical metrics

Calculating precision (TA1, TA2)

The ultimate goal of this programme is to develop circuit-level neurotechnologies. To capture how well a technology interfaces with neural circuits, we have developed the following 'precision' metric which will be the focus of TA1 and TA2. It comprises four components (see Figure 2):

1. Cell type specificity (S)
   To capture cell type specificity we define the unitless quantity $S = n/T$, where n is the number of cell type specific neurons that contribute to the recorded/written signal and T is the total number of neurons contributing to the recorded/written signal. For example, if the intended modulation target are GABAergic interneurons and $n = 5$ are modulated in a particular volume, but 2 non-interneurons are also modulated, then $S = 5/(5 + 2) = 0.7$. For technologies with no cell type specificity, we define $S = 0.5$. We acknowledge cell type can be defined in a number of ways (functionally, morphologically, transcriptomically) and leave it up to teams to select their working definition.

2. Volume of interaction (V)
   A smaller volume of interaction enables distinct circuit elements to be individually addressed and to minimise off-target effects. The term 'volume of interaction' is intended to capture the functional volume that is directly recorded/written, rather than simply the integrated field.

3. Field of view (F)
   Field of view refers to the maximum addressable volume across the brain. We define it volumetrically to account for differences between e.g. axial and lateral fields of view. We particularly encourage technologies that can span both cortical and subcortical regions.

4. Maximum voxel number (N)
   Increasing the maximum number of addressable targets enables multiple brain regions or micro-circuit elements to be targeted simultaneously.

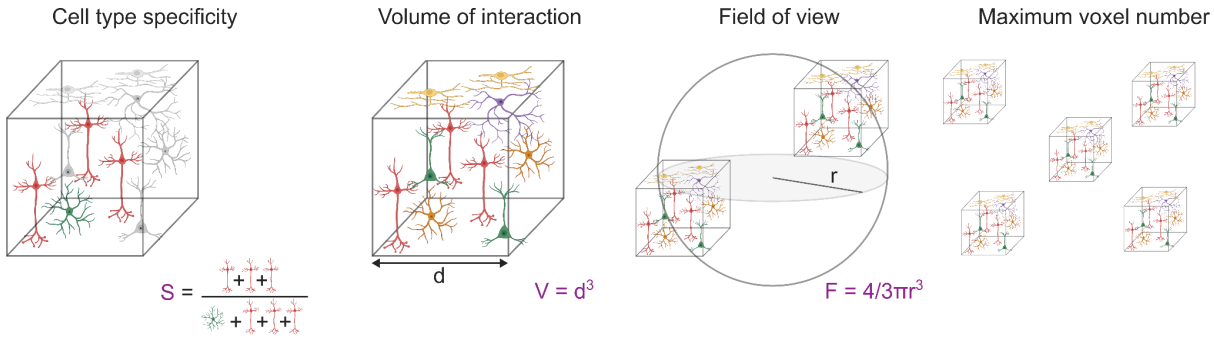

Figure 2. *Metrics to capture circuit-level neural interfaces. While we believe that simultaneous advances in all these areas are important, we anticipate (and encourage) certain technology platforms to spike against particular performance metrics, e.g. a technology X that significantly increases volumetric coverage, or a technology Y that significantly increases cell type specificity.*

The first two elements, S and V, refer to the signal 'localisation' of a neurotechnology, while F and N refer to the 'scale' of a neurotechnology (see Figure 4). We now combine these elements via the L2-norm to define a 'precision metric':

$$P = \sqrt{|(F/V_{cns}) \times Log_{10}(N)|^2 + |S \times Log_{10}(V/V_{cns})|^2},$$

where V_{cns} = 1200 cm^3 is the volume of the human central nervous system [28].

Example calculation:

Consider a four-lead DBS system that can be implanted in 90% of the volume of the human brain. Assuming that the volume of tissue activated by each lead is 70 mm^3 and that there is no cell type selectivity of modulation:

$$P = \sqrt{|0.9 \times Log_{10}(4)|^2 + |0.5 \times Log_{10}(0.07/1200)|^2}$$
$$P = \sqrt{|0.54|^2 + |-2.12|^2}$$
$$P = 2.19$$

The pareto frontier of existing technologies are shown in Figure 3 alongside the target for the programme, which simultaneously increases the number of addressable targets by an order of magnitude, decreases the volume of interaction by an order of magnitude, has full volumetric access to the brain and approaches near-unity cell type specificity.

Note, 'neural activity' is intended to capture a variety of neural signals, which may include single unit or bulk electrical responses but also other biologically relevant signals such as neurotransmitter concentration or hemodynamic activity.

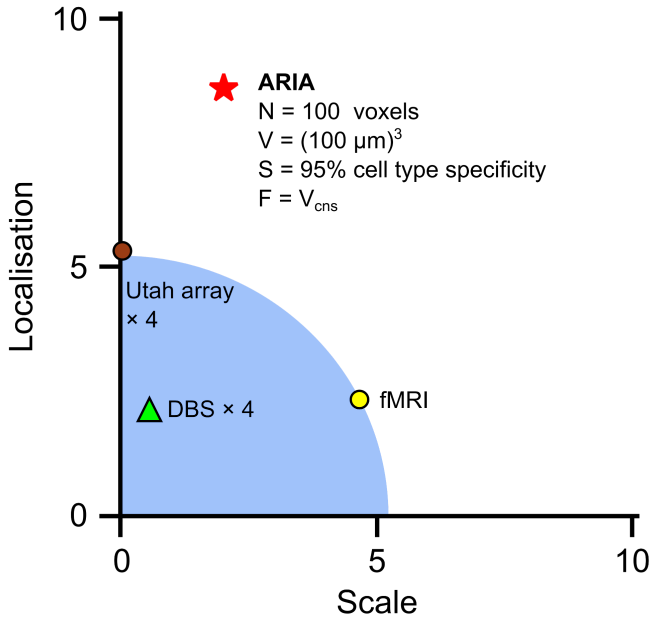

***Figure 3**. Pareto frontier of precision neurotechnologies. The individual components of scale and localisation are plotted for three different state-of-the art technologies: four implanted DBS leads [29], fMRI [30], four implanted Utah arrays [31]. The precision target for this programme (red star) is also plotted.*

Measuring precision (TA1, TA2)

Teams will be tasked with measuring precision during the programme. Therefore, during the application stage, we require teams to describe their plans. Approaches may include but are not limited to:

+ Optical imaging of genetically encoded indicators for cell type specific readout.
+ Electrophysiology.
+ Multiphysics computational modelling.
+ Any other techniques that can give ground truth measurement of precision.

Calculating correlation (TA2)

The goal of TA2 is to integrate precision neurotechnologies into a measure-model-perturb cycle to demonstrate the controllable, predictable and reversible transition between novel brain states, *in vivo*. To quantify how well a technology can transition to target brain state teams will be tasked with selecting a set of $N > 2$ brain states and measuring the mean correlation between target time-series $\{x_t\}$ and actual time-series $\{y_t\}$ of brain states in the presence of neuromodulation:

$$\rho(x,y) = [\sum_t (x_t - \overline{x})(y_t - \overline{y})] / \sqrt{\sum_t (x_t - \overline{x})^2 (y_t - \overline{y})^2}$$

In addition, the necessary statistical tests and controls will be required, such as cross validation and comparison to a properly shuffled time series distribution (see e.g. [32]).

The target of this programme is to reach a mean $\overline{\rho} = 0.6$ over the set of N brain states, where the current state-of-the-art for prediction only (rather than transitioning to a target state) is $\rho = 0.45$ [17].

SECTION 4: What are we looking for/what are we not looking for

We are interested in approaches that leverage insights from biology, apply methods in biological engineering or bring together engineered biology with engineered hardware. Examples include (but are not limited to):

+ Bio-hybrid approaches including those based on functionalised bioelectronics [33] or stem cells [34].
+ Cell type specific gene therapies [35] that can be actively controlled, e.g., based on activity or chemogenetics [36].
+ Blood based neuromodulation and neuromonitoring [37].
+ Nanotransducer networks controlled by external magnetic, optical, or acoustic fields [38].
+ Next-generation focused ultrasound systems with cell type specific [39], multi-site [40] and/or spatially precise [41] neuromodulation and recording.
+ Any other technological approach that can conceivably meet the desired programme targets.

We are also interested in approaches that leverage novel surgical or delivery methods. Examples include (but are not limited to):

+ Injectables [23].
+ Skull implants (compatible with standard burr hole geometries) [24].
+ Neuroendovascular stents [25].

Technologies that are likely out of scope:

+ Incremental advances of existing technologies.
+ Approaches that cannot be made portable, e.g. large-scale facilities such as fMRI or benchtop microscopy. Note, large-scale facilities are allowed to be used during development, such as for benchmarking and ground truth measurements, or on the referral pathway.
+ Technologies that lack a clear pathway towards demonstrating safety for use in humans.

SECTION 5: Programme duration and project management

The maximum term of the programme is four years, though applicants are encouraged to consider plans which may reach success (or failure) on faster timelines. Teams selected at the full proposal stage will enter into a contracting phase with ARIA where the specific scope of work will be finalised. This phase will require updated and more accurate cost assessments for the proposed project.

Project Milestones

Each project's progress will be monitored using clearly defined milestones. Milestones will be defined by the applicant prior to the start of a project, be agreed upon by ARIA, and should be designed to easily convey progress to a third party. In order to do this, milestones should:

+ Be specific, measurable, and signify a meaningful step towards reaching the overall programme goals.
+ Include details on methods used for measurement and evaluation.
+ Be defined on a quarterly cadence for all phases of the Programme.
+ Include major "Go / No-Go" decision points.

Success/pivot/closure criteria for each project will be determined by the applicant's ability to meet these agreed-upon milestones.

Programme & project management

During each quarterly site-visit, project teams and the ARIA Programme Director will review the agreed upon Milestones, and discuss further details of each project. As part of that discussion, teams will be encouraged to think through the following questions as they execute on their plan:

+ What is(are) the target deliverable(s) for each phase of the programme?
+ What are the top three risks identified at this stage of the project?
+ What are the first three experiments required to overcome each risk?
+ What are the expected outcomes/learnings from these experiments?
+ How long will these experiments take and how much will they cost?
+ What are the dependencies from prior activities/phases of the Programme?

Upon completion of each experiment, questions we will look to answer are:

+ What new information has been gleaned?
+ What (if any) risks have been overcome? What new risks have emerged?
+ Did we learn what we thought we would learn? If not, why not?
+ Is there anything we can do to learn more or faster?
+ Is there still a path towards the target? Are we heading towards any dead ends?

Community events

In an effort to foster a collaborative research environment, ARIA will host regular community events to allow all programme teams to exchange updates, ideas, and feedback on best paths forward. ARIA will also host annual in-person workshops where teams can showcase their work to a wider research community.

SECTION 6: Eligibility & application process

Eligibility

We welcome applications from across the R&D ecosystem, including individuals, universities, research institutions, small, medium and large companies, charities and public sector research organisations.

Lead applicants can submit multiple applications for Technical Area 1 and 2 (provided they are materially different) but will only be eligible to lead an award in either Technical Area 1 or Technical Area 2, not both. If you submit proposals for both Technical Area 1 or Technical Area 2, please indicate your preference for receiving an award in the event both proposals are reviewed favourably. Individuals, teams or organisations can however be *supporting* collaborators on multiple proposals in any technical area.

Lead applicants can also choose to submit proposals for Technical Area 3 even if they have submitted a proposal for Technical Area 1 or Technical Area 2, this does not affect your eligibility for an award under Technical Area 1 or 2.

Our primary focus is on funding those who are based in the UK. For the vast majority of applicants, we therefore require the majority of the project work to be conducted in the UK (i.e. >50% of project costs and personnel time).

However, we can award funding to applicants whose projects will primarily take place outside of the UK, if we believe it can boost the net impact of a programme.

In these instances, you must outline any proposed plans or commitments in the UK that will contribute to the programme within the project's duration (note the maximum project duration is 4 years). If you are selected for an award subject to negotiation, these plans will form part of those negotiations and any resultant contract/grant.

More information on the evaluation criteria we will use to assess benefit to the UK can be found later in the document here.

Finding potential collaborators and teaming

For those seeking specific expertise to support their proposal, we have created a teaming request form to facilitate finding potential team members who have registered their interest in this programme. By following the link to the sign up form here you will be able to register, submit your details, and gain access to a list of other individuals seeking to

find/share their expertise. All requests are screened via ARIA's internal team prior to access, after which connections will be made by individual users based on aligned expertise.

Application process

The application process for Technical Areas 1, 2 and 3 consists of two stages:

Stage 1 - Concept paper

Concept Papers are designed to make the solicitation process as efficient as possible for applicants. By soliciting short concept papers (no more than three pages) ARIA reviewers are able to gauge the feasibility and relevance of the proposed project and give an initial indication of whether we think a full proposal would be competitive. Based on this feedback you can then decide whether you want to submit a full proposal. You can find out more about ARIA's review process here.

If you miss the deadline for submission of concept papers you can still submit a full proposal. However, we strongly encourage you to submit a concept paper. On average, only 8% of applicants that do not submit a concept paper are selected for award.

To ensure the process is quick and open we do not require your organisation's consent prior to submission of a concept paper.

You can find guidance on what to include in a concept paper here.

Following review of concept papers applicants will either be encouraged or discouraged from submitting a full proposal. For more details on the evaluation criteria we'll use, click here.

Stage 2 - Full proposals

This step requires you to submit a detailed proposal including:

- **Project & Technical information** to help us gain a detailed understanding of your proposal.
- **Information about the team** to help us learn more about who will be doing the research, their expertise, and why you/the team are motivated to solve the problem.
- **Administrative questions** to help ensure we are responsibly funding R&D. Questions relate to budgets, IP, potential COIs etc. Where you are proposing to

conduct any animal testing or clinical trials as part of your proposed project you'll be required to answer some additional questions in the section.

You can find more detailed guidance on what to include in a full proposal here. **You can submit a full proposal even if you did not submit a concept paper.**

For more details on the evaluation criteria we'll use, click here.

SECTION 7: Timelines

This call for project funding will be open for applications as follows (timelines may be updated based on the volume of responses received):

Applications open	**10 July 2024**
Concept paper submission deadline	**29 July 2024 (12:00 BST)**
Concept paper review & notification of encouraged/not encouraged to submit full proposal sent	**29 July — 9 August 2024**
At this stage and based on your concept paper, you will either be encouraged/ discouraged to submit a full proposal. If you receive feedback indicating that you are not encouraged to submit a full proposal you can still choose to submit a full proposal. You should note that this preliminary assessment/encouragement provides no guarantee of any full proposal being selected for award of funding.	
Full proposal submission deadline	**9 September 2024 (12:00 BST)**
Full proposal review	**10 September - 28 October 2024**
As part of our review we may invite applicants to meet with the Programme Director to discuss any critical questions/concerns prior to final selection — this discussion can happen virtually or we may seek clarification on certain aspects of your proposal via email.	
Successful/Unsuccessful applicants notified	**30 October 2024**
At this stage you will be notified if you have or have not been selected for an award	

subject to due diligence and negotiation. If you have been selected for an award (subject to negotiations) we expect a 1 hour initial call to take place between ARIA's PD and your lead researcher within 10 working days of being notified.

We expect contract/grant signature to be no later than 8 weeks from successful/ unsuccessful notifications. During this period the following activity will take place:

- Due diligence will be carried out.
- The PD and the applicant will discuss, negotiate and agree the project activities, milestones and budget details.
- Agreement to the set Terms and Conditions of the Grant/Contract. You can find a copy of our funding agreements here.

SECTION 8: Evaluation criteria

Concept paper and proposal evaluation principles

To build a programme at ARIA, each Programme Director directs the review, selection, and funding of a portfolio of projects, whose collective aim is to unlock breakthroughs that impact society. As such, we empower Programme Directors to make robust selection decisions in service of their programme's objectives ensuring they justify their selection recommendations internally for consistency of process and fairness prior to final selection.

We take a criteria-led approach to evaluation, as such all proposals are evaluated against the criteria outlined below. We expect proposals to spike against our criteria and have different strengths and weaknesses. Expert technical reviewers (both internal and external to ARIA) evaluate proposals to provide independent views, stimulate discussion and inform decision-making. Final selection will be based on an assessment of the programme portfolio as a whole, its alignment with the overall programme goals and objectives and the diversity of applicants across the programme.

Further information on ARIA's proposal review process can be found here.

Proposal evaluation process and criteria

Proposals will pass through an initial screening and compliance review to ensure proposals conform to the format guidance and they are within the scope of the solicitation. At this stage we will also carry out some checks to verify your identity, review

any national security risks and check for any conflicts of interest. Prior to review of applications Programme Directors and all other reviewers are required to recuse themselves from decision making related to any party that represents a real or perceived conflict.

Where it is clear that a proposal is not compliant and/or outside the scope, these proposals will be rejected prior to a full review on the basis they are not compliant or non-eligible.

Proposals that pass through the initial screening and compliance review will then proceed to full review by the Programme Director and expert technical reviewers.

In conducting a full review of the proposal we'll consider the following criteria:

1. **Worth shooting for** – The proposed project uniquely contributes to the overall portfolio of approaches needed to advance the programme goals and objectives. It has the potential to be transformative and/or address critical challenges within and/or meaningfully contribute to the programme thesis, metrics or measures.

2. **Differentiated** – The proposed approach is innovative and differentiated from commercial or emerging technologies being funded or developed elsewhere.

3. **Well defined** – The proposed project clearly identifies what R&D will be done to advance the programme thesis, metrics or measures, is feasible and supported by data and/or strong scientific rationale. The composition and planned coordination and management of the team is clearly defined and reasonable. Task descriptions and associated technical elements provided are complete and in a logical sequence with all proposed stage-gates and deliverables clearly defined.

4. **Responsible** – The proposal identifies major ethical, legal or regulatory risks and that planned mitigation efforts are clearly defined and feasible.

5. **Intrinsic motivation** – The individual or team proposed demonstrates deep problem knowledge, have advanced skills in the proposed area and shows intrinsic motivation to work on the project. The proposal brings together disciplines from diverse backgrounds.

6. **Benefit to the UK**

There is a clear case for how the project will benefit the UK. Strong cases for benefit to the UK include proposals that:

1. are led by an applicant within the UK who will perform the majority (>50% of project costs spent in the UK) of the project within the UK
2. are led by an applicant outside the UK who seeks to establish operations inside the UK, perform a majority (>50% of project costs spent in the UK) of the project inside the UK and present a credible plan for achieving this within the programme duration.

For all other applicants we will evaluate the proposal based on its potential to boost the net impact of the programme in the UK. This could include:

3. A commitment to providing a direct benefit to the UK economy, scientific innovation, invention, or quality of life, commensurate with the value of the award;
4. The project's inclusion in the programme significantly boosts the probability of success and/or increases the net benefit of specific UK-based programme elements, for example, the project represents a small but essential component of the programme for which there is no reasonable, comparably capable UK alternative.

When considering the benefit to the UK, the proposal will be considered on a portfolio basis and with regard to the next best alternative proposal from a UK organisation/individual.

Where applicants propose animal research involving non-human primates, cats, dogs, equines, and pigs as part of their project, ARIA will share the relevant parts of proposals shortlisted following stage 2 full proposal with NC3R for expert review.

SECTION 9: How to apply

Before submitting an application we strongly encourage you to read this call in full, as well as the general ARIA funding FAQs.

If you have any questions relating to the call, please submit your question to clarifications@aria.org.uk.

Clarification questions should be submitted no later than four days prior to the relevant deadline date. Clarification questions received after this date will not be reviewed. Any questions or responses containing information relevant to all applicants will be provided to everyone that has started a submission within the application portal. We'll also periodically publish questions and answers on our website, to keep up to date click here.

Please read the portal instructions below and create your account before the application deadline. In case of any technical issues with the portal please contact clarifications@aria.org.uk.

Application Portal instructions.

APPLY HERE.

SECTION 10: References

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